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QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE, SUITE 2040
MILWAUKEE, WI 53202-4497

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/711,517
Filing Date: September 23, 2004
Appellant(s): ABBOTT ET AL.

Keith Heidmann
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/2/2009 (and as corrected on 2/12/2009) appealing from the Office action mailed 12/4/2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

- Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-23 of copending Application No. 11/542,432 in view of Renault et al.
- Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-34 of copending Application No. 11/418,755 in view of Renault et al.

See the Office action mailed 12/4/2007 at pages 12-15.

Appellant's Appeal Brief does not include the above provisional rejections in the listing of Grounds of Rejection to be Reviewed on Appeal, and Appellant has failed to argue the rejections.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,284,197	ABBOTT	9-2001
5,886,195	TANG	3-1999
6,292,296	CHOI	9-2001

Bernard, A. et al. "Affinity capture of proteins from solution and their dissociation by contact printing" Nature Biotechnology, vol19 (September 2001), pp. 866-869.

Renault, J.P. et al. "Fabricating Microarrays of Functional Proteins Using Affinity Contact Printing" Angew. Chem. Int. Ed. vol. 42, no. 13 (2002), pp. 2320-2323.

Supporting Information accompanying Renault, J.A. et al. ("Fabricating Microarrays of Functional Proteins Using Affinity Contact Printing", vol. 41, no. 13 (2002), pp. 2320-2323), retrieved from the publisher's website at http://www.angewandte.org (2002), 2 pages.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-6, 10-11, 15-20 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 1 recites:

> (c) detecting the presence of the ligand on the detection surface by contacting the detection surface with a liquid crystal, wherein the presence of the ligand on the detection surface is detected ***by a change in the orientation of the liquid crystal*** contacted with the detection surface.

(emphasis added)

The claim is indefinite because it is not clear what the change in liquid orientation is being assessed relative to. Previous versions of the claim recited that the detection surface already included a liquid crystal prior to application of the ligand. Therefore, reference to a "change" was meaningful in the context of before-and-after ligand binding to the detection surface.

However, the claim now reads on methods in which the ligand is applied to the detection surface first and then the liquid crystal is subsequently applied to the surface. In this case, it is not clear what the change in orientation would be assessed relative to, since the liquid crystal would not yet be oriented or anchored on the surface before ligand binding.

Therefore, it is not clear how a "change" in orientation would be assessed. For example, is the change relative to the orientation of liquid crystals on a control detection surface having no printed ligand? Relative to other areas of the surface not contacted by the affinity substrate? Or relative to the orientation of the liquid crystals before they are contacted with the surface?

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-6, 10-11, 15-20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Bernard et al. ("Affinity capture of proteins from solution and their dissociation by contact printing" (2001) *Nature Biotechnology* **19**:866-869) or alternatively over Renault et al. (*Agnew. Chem. Int. Ed.* 2002, 41, No. 13, 2320-2323, Applicant's IDS of 1/30/2006 and the accompanying Supporting Information for the article obtained from http://www.angewandte.org on 3/21/07) in view of Abbott et al. (US 6,284,197 B1, Applicant's IDS of 1/30/2006).

Bernard et al. teach a method for detecting a ligand comprising (a) contacting a sample having a ligand ("target molecule", for example ^{125}**I-IgG**) with an affinity substrate (polydimethylsiloxane (PDMS) stamp), wherein the affinity substrate comprises receptors ("capturing molecules") that are capable of specifically binding the ligand. The receptors are for example anti-mouse IgGs, which is capable of specifically binding to IgG. Bernard et al. also teach that the affinity substrate could be patterned with various different types of capturing molecules in order to screen for several ligands in a parallel manner (see the paragraph bridging pages 868-869). See entire selection, in particular the abstract; Figures 1-2 and p. 866, left

column and the paragraph bridging the left and right columns; and p. 869, "Derivatization of stamps".

Bernard et al. further teach (b) contacting the affinity substrate with a detection surface (glass or polystyrene), wherein at least a portion of the ligand that is bound to the receptor is transferred to the detection surface (see in particular p. 866, left column, second paragraph; p. 867, left column; Figure 3; the first paragraph of "Results and Discussion" on p. 866; and also p. 869, "Affinity stamping").

Bernard et al. differs from the claimed invention in that it fails to specifically teach detecting the presence of the ligand by contacting the detection surface with a liquid crystal, wherein a change in the orientation of the liquid crystal indicates the presence of a ligand. By contrast, in Bernard et al., the printed ligands are detected using radioactive or fluorescent labels attached to the target ligands (see especially p. 866, right column; p. 869, right column; and Figures 2 and 4).

Like Bernard et al., Renault et al. similarly teaches an affinity capture method followed by microcontact printing. In particular, Renault et al. teaches a method for detecting ligands ("target molecules", e.g. antibodies) by contacting a sample (e.g., solution containing target antibodies) with an affinity substrate (PDMS elastomeric stamp) (see entire selection, especially p. 2320, left column and the paragraph bridging the left and right columns; p. 2323, left column, last paragraph; and Figures 1, 2d, and 3-4). The affinity substrate comprises an array of receptors ("capture molecules") on the substrate, defining various capture sites that each have different capture molecules capable of specifically binding to different target proteins (see depiction in

Figure 1A; p. 2321, right column and also p. 2320, the paragraph bridging the left and right columns).

Renault et al. further teach contacting the affinity substrate with a detection surface ("substrate", which was glass in the examples); see also p. 2322, left column. This results in the captured target molecules being transferred onto the substrate (see depiction in Figure 1E).

However, like Bernard et al., the teachings of Renault et al. differ from the claimed invention in that the reference fails to specifically teach detecting the presence of the ligand by contacting the detection surface with a liquid crystal, wherein a change in the orientation of the liquid crystal indicates the presence of a ligand. As in Bernard et al., detection of the presence of the ligand on the detection surface was performed using labeled target molecules. Specifically, Renault et al. teach detection of fluorescent- or gold-labeled antibodies by fluorescence microscopy or atomic force microscopy, respectively (see especially Figure 5).

Abbott et al. teach devices and methods for detecting a ligand based on the use of liquid crystals to amplify and transduce into an optical signal the interaction of a wide array of molecules with various surfaces (see entire selection, in particular the abstract; column 4, line 49 to column 5, line 26).

To perform liquid crystal detection, the ligand is bound to the surface of the substrate, liquid crystal is contacted with the substrate in the form of a mesogenic layer, and the orientation of the liquid crystal is assessed. See in particular the abstract; column 30, line 29 to column 32, line 29 (and especially at column 32, lines 21-29); claim 1, step (b) in particular; and Example 1. In other embodiments, the ligand may be bound to the surface of liquid crystal devices in which

the liquid crystal is already coupled to the surface (column 13, lines 4-25; and column 5, line 13 to column 6, line 14).

The liquid crystal (mesogens) undergo a detectable switch in orientation upon interaction of the ligand with the surface, allowing for the ligand to be detected (column 5, line 13 to column 6, line 3; column 13, lines 3-31; column 14, lines 15-43; column 20, lines 4-12; column 38, line 46 to column 39, line 50).

Abbott et al. teach that the use of liquid crystals in devices to detect allows for simple, inexpensive, and reliable detection and characterization of analytes (column 4, line 61 to column 5, line 10). Such easily detected optical output even allows for changes in the mesogenic layer to be easily seen with the naked eye (column 5, lines 18-27). Moreover, Abbott et al. teach that liquid crystal detection obviates the need for prelabeling of ligand, such as with a radiolabel or a fluorescent moiety (see column 5, lines 5-10).

Therefore, it would have been obvious to one of ordinary skill in the art to employ liquid crystal detection as taught by Abbott et al. in place of fluorescent, gold, or radioactive labeling-based detection as the means of detecting the ligand in the methods of Bernard et al. or Renault et al. In particular, it would have been obvious to subsequently contact the ligand-printed detection surfaces of Bernard et al. or Renault et al. with a liquid crystal (e.g., in the form of an organic mesogenic layer) as taught by Abbott et al. and to detect the presence of the ligand on the surface via a change in the liquid crystal orientation. As the methods of Bernard et al. and Renault et al. each involve binding ligands to a surface by affinity microcontact printing, it would have been obvious to combine the reference teachings in this manner because Abbott et al.

taught that ligands bound to a surface may be detected by subsequently contacting the surface with a liquid crystal.

One would have a reasonable expectation of success because the detection surfaces taught by Renault et al. and Bernard et al. (glass and/or polystyrene) are taught by Abbott et al. as suitable substrates for liquid crystal detection (see Abbott et al. at column 14, line 44 to column 16, line 14).

In addition, since claim 1 does not require a particular order in which the liquid crystal is contacted with the liquid crystal (as recited in step (c)), this means that the detection surface could be contacted with the liquid crystal prior to application of the ligand. Therefore, it would also have been obvious to arrive at the claimed invention by employing the liquid crystal devices of Abbott et al. (having liquid crystal already coupled to the substrate surface) as the detection surface on which the ligand is microcontact printed and to detect the ligand by a change in orientation of the liquid crystal in the methods for detecting a ligand of either Bernard et al. or Renault et al. One would also have had a reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the method of Bernard et al. or Renault et al. because the surface of Abbott et al. is compatible with microcontact printing (see column 17, lines 1-18).

One would be motivated to combine the reference teachings in either of the two ways as discussed above because Abbott et al. teach that liquid crystal detection surfaces do not require prelabeling of the ligand (as was performed in Bernard et al. and Renault et al.) and allow for an easily detected optical output, including even detection by naked eye. As such, one would be motivated to stamp the affinity-captured ligand onto the device of Abbott et al. in order to avoid the need for using fluorescent or other labels on the ligands. Similarly, one would be motivated

to apply a liquid crystal to the affinity-printed surfaces of Bernard et al. or Renault et al. in order to avoid the need to use labeled ligands.

With regard to claim 2, Bernard et al. teach (a) washing the affinity substrate after the contacting step (a) above (p. 869, "Affinity stamping"). Renault et al. also teach (a) rinsing the stamp after contacting it with the sample (see especially the legend to Figure 2).

With regard to claims 4-5, Bernard et al. teach affinity substrates consisting of PDMS as an inert elastomer (p. 866, left column, paragraph 3). Renault et al. also teaches a PDMS elastomeric stamp (see especially p. 2320, left column).

With respect to claim 6, the PDMS affinity substrates of Bernard et al. are "antibody-terminated" in that the antibodies are attached to the ends of PDMS stamps (Figure 1). The antibodies are capable of binding to a protein (^{125}I-IgG). Bernard et al. teach the use of antibodies in this context as capturing molecules (e.g., see p. 866, first two paragraphs of "Results and Discussion"). Similarly, Renault et al. teach attaching the capture molecules (which may be antibodies) to the surface or end of the PDMS stamps (Figure 1 and p. 2320-2321).

With regard to claim 10, Bernard et al. teach that the antibodies, protein A, and streptavidin were applied to the affinity stamps via the cross-linker BS3 (p. 869, "Derivatization of stamps"). Renault et al. similarly teach that the receptors are attached via this same crosslinker (p. 2320, right column).

With regard to claim 11, while not specifically recited by Bernard et al., the amount of ligand present in the sample was necessarily quantified because Bernard et al. teach the concentrations of the ligands TRITC-labeled rabbit IgG and biotinylated alkaline phosphatase in the samples (see p 869, "Affinity Stamping and Figure 2A). Similarly, Renault et al. report the

quantity of the ligand in the sample (see Supporting Information, page 1), such that the ligand was necessarily quantified.

With regard to claims 15-17 and 19, Abbott et al. further teach that the detection surface may comprise self-assembled monolayers in order to anchor the liquid crystal mesogenic layer, where the self-assembled monolayers may be formed from alkanethiols or organosulfur compounds and may comprise amines through functionalization (the abstract; column 19, line 25 to column 21, line 16). Abbott et al. teach that use of certain self-assembled monolayers enables homeotropically anchoring of mesogens, and that homeotropic anchoring is the most preferred anchoring direction (see especially column 18, line 4, to column 19, line 45). Abbott et al. teach that the detection surface may be treated with 1-aminododecanoic acid to make the surface surface-active (column 25, lines 26-31).

With regard to claim 18, the specification discloses that "The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, *such that at least a portion of the first surface is partially curved"* (paragraph 28, emphasis added). Thus, the specification indicates that partial curvature of the affinity substrate occurs as a result of contacting the affinity substrate with a surface. In the absence of any specific structural limitations recited, the methods of Bernard et al. or Renault et al. and Abbott et al. meet the claim since in the course of contacting the affinity substrates of Bernard et al. or Renault et al. with the detection surface of Abbott et al., the surface of the affinity substrates would become partially curved as indicated by the specification.

With regard to claims 20 and 22, the liquid crystal mesogens of Abbott et al. may be thermotropic or lyotropic and may be nematic, chiral nematic, smectic, frustrated liquid crystals, or discotic liquid crystals (column 30, line 30 to column 32, line 29), and a preferred liquid crystal is 4-cyano-4'-pentylbiphenyl (5CB) (column 37, lines 53-59).

With regard to claim 23, Abbott et al. teach that the detection surface allows for optical detection of orientation of the liquid crystal (mesogens), which allows for ease of detection (column 5, lines 13-26). Electrical detection may also be employed (column 38, lines 56-63).

7. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. or Renault et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Tang et al. (US Patent No. 5,886,195).

Bernard et al., Renault et al., and Abbott et al. are as discussed above, which fail to specifically teach a method wherein the receptor is capable of detecting the presence of protein phosphorylation in EGFR residues.

Tang et al. teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity (column 6, lines 53-65).

Therefore, it would have been obvious to one of ordinary skill in the art to employ anti-phosphotyrosine antibodies as taught by Tang et al. as the capturing molecule on the PDMS affinity substrates in the method for detecting a ligand of Bernard et al. and Abbott et al., or alternatively of Renault et al. and Abbott et al., in order to measure autophosphorylation of EGFR residues. One would have reasonable expectation of success because Bernard et al. and Renault et al. teach that antibodies can be used as capture molecules on PDMS stamps.

8. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. or Renault et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Choi et al. (US 6,292,296).

Bernard et al., Renault et al., and Abbott et al. are as discussed above, which fail to treat a method wherein the liquid crystal is pretreated by illumination with UV light.

Choi et al. teach methods for aligning liquid crystal devices, including rubbing as well as photo-alignment using ultraviolet light (column 1, lines 10-51). The reference teaches that compared with the rubbing method, there is no electrostatic discharge or dust particles associated with photo-alignment, thus obviating low yield problems.

Therefore, would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the liquid crystal detection surface of Abbott et al. by photo-alignment with ultraviolet light as taught by Choi et al. (rather than by rubbing as exemplified by Abbott et al.; see column 16, lines 52-53), in the method of Bernard et al. (or Renault et al.) and Abbott et al. order to align the liquid crystal detection surface while avoiding disadvantages such as dust particles that are known to be associated with the rubbing method.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-23 of copending Application No. 11/542,432 in view of Renault et al.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '432 application also claims a method for detecting a ligand (analyte) in which an affinity substrate ("affinity stamp") is used to transfer a captured analyte from the stamp to a detection surface ("substrate surface") by microcontact printing (see especially claims 18-19). Although the '432 application fails to specifically recite that the affinity substrate is contacted with a sample having or suspected of having the ligand, such a step would be immediately envisaged since the claims recite a method of detecting an analyte *in a sample*. The '432 application further recites the step of detecting the presence of the ligand by introducing a liquid crystal to the detection surface and detecting a change or departure in the orientation of the liquid crystal (see especially claim 18, steps (b)-(c) and claims 22-23).

The '432 application differs from the claimed invention in that it fails to specifically recite that the affinity substrate comprises an array of receptors, wherein each receptor is capable of specifically binding to a ligand.

However, Renault et al. teaches methods of transferring captured analytes from affinity stamps by affinity microcontact printing. The reference teaches assembling an "array" of various types of capturing molecules on the surface of a stamp (see especially Figure 1 and p. 2320, the paragraph bridging the left and right columns). The reference teaches that this allows simultaneous capture of different target proteins from a complex solution (ibid).

Therefore, it would have been obvious to one of ordinary skill in the art to provide the affinity stamp of the '432 application with an array of receptors in order to enable simultaneous capture of different target proteins from a complex solution.

11. Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-34 of copending Application No. 11/418,755 in view of Renault et al.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '755 application also claims a method for detecting the presence of an analyte in a sample suspected of containing the analyte by exposing the sample with an affinity substrate (stamp comprising a pad functionalized with a ligand) and then contacting the affinity substrate with a detection surface ("detection region") (see especially claim 21). The presence of the analyte on the detection region is determined by contacting the detection surface with a mesogen to form a liquid crystal and detecting a change in the orientation ("ordering") of a liquid crystal (see step (6) of claim 21 and also claim 34).

The '755 application differs from the claimed invention in that it fails to specifically recite that the affinity substrate comprises an array of receptors, wherein each receptor is capable of specifically binding to a ligand.

However, Renault et al. teaches methods of transferring captured analytes from affinity stamps by affinity microcontact printing. The reference teaches assembling an "array" of various types of capturing molecules on the surface of a stamp (see especially Figure 1 and p. 2320, the paragraph bridging the left and right columns). The reference teaches that this allows simultaneous capture of different target proteins from a complex solution (ibid).

Therefore, it would have been obvious to one of ordinary skill in the art to provide the affinity stamp of the '432 application with an array of receptors in order to enable simultaneous capture of different target proteins from a complex solution.

The above are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

(10) Response to Argument

Appellant's arguments as set forth in the Replacement Argument Section submitted on 2/12/2009 have been fully considered but are not persuasive of error.

With respect to the rejections of claims 1-6, 10-11, 15-20 and 22-23 under 35 U.S.C. 112, second paragraph, ***Appellant argues that the Office has erred in not considering the meaning of the rejected claims in light of the specification*** (see Replacement Argument Section

submitted on 2/12/2009 at pages 3-5, numbered item 2, and in particular at page 4, paragraphs 2-4).

In particular, Appellant argues that the recitation of "a change in the orientation of the liquid crystal contacted with the detection surface" is meaningful in view of the disclosure of paragraph [0055] that a disordering or disruption of the liquid crystal on a detector surface (i.e., inconsistent orientation of the liquid crystal) indicates the presence of the ligand. Appellant also points to Figure 1.1, which depicts that the orientation of the liquid crystal in contact with regions of the detection surface containing bound ligand ***relative to*** the orientation of liquid crystal in contact with regions of the same detection surface that do not contain ligand (Replacement Argument Section of 2/12/2009 at page 4, third paragraph). Similarly, Appellant also points to Figure 3 and paragraph [0208], in which a difference in the orientation between the liquid crystal in contact with the printed regions ***as compared to*** the orientation of the liquid crystal in contact with the non-printed regions was observed ((Replacement Argument Section of 2/12/2009 at page 4, fourth paragraph).

This is not found persuasive because although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant urges that the "change in the orientation of the liquid crystal contacted with the detection surface" is assessed *relative to* or *as compared to* the orientation of liquid crystal in contact with regions of the same detection surface that do not contain ligand.

However, such a limitation is not recited in the claims, which do not specify what the change in orientation is *relative to* or *as compared to*.

In addition, other plausible constructions of the "change in orientation" are possible. For example, this claim language could also refer to the orientation of the liquid crystals prior to their application onto the detection surface vs. their orientation after being applied to the detection surface.

In summary, because multiple plausible constructions of the claims are possible, and because limitations of the specification cannot properly be read into the claims, it is maintained that the claims are indefinite because they do not recite a frame of reference or standard for understanding what the change in orientation of the liquid crystal is relative to.

With respect to the rejections of claims 1-6, 10-11, 15-20 and 22-23 under 35 U.S.C. 103(a) as being unpatentable over either Bernard et al., or, alternatively, over Renault et al. and the accompanying Supporting Information, in view of Abbott et al., Appellant's arguments are summarized as follows (see the Replacement Argument Section submitted on 2/12/2009 at page 6, first full paragraph):

(1) *The Examiner has not properly considered the evidence of the Abbott Declaration*

(2) *The skilled artisan would not have had a reasonable expectation of success in combining the cited documents to practice the claimed method*

(3) *The skilled artisan would have had no motivation to combine the cited documents to practice the claimed method*

(4) *The rejection is improperly based upon hindsight reconstruction*

Regarding argument **(1)** above, Appellant argues that the Office did not address the substance of the Abbott Declaration filed under § 1.132 on October 10, 2007 (Evidence Appendix B). See the Replacement Argument Section submitted on 2/12/2009 at pages 6-9, item 3.

This is not found persuasive because the evidence presented in the Abbott Declaration was fully considered by the Examiner, but was nonetheless not found persuasive to outweigh the evidence of obviousness because it attempted to rebut a position which has not been taken by the Office. The Declaration was not dismissed but rather addressed at length in the Office action mailed 12/4/2007 (see pages 15-17).

At issue is the reference to "microcontact printing" by Abbott et al. (U.S. 6,284,197[1]), which is the secondary reference being relied upon in the rejections under 35 U.S.C. 103(a).

At column 17, lines 1-6, Abbott et al. disclose:

> The substrate can also be patterned using techniques such as photolithography (Kleinfield et al., J. Neurosci. 8:4098-120 (1998)), photoetching, chemical etching and **microcontact printing** (Kumar et al., Langmuir 10:1498-511 (1994)). Other techniques for forming patterns on a substrate will be readily apparent to those of skill in the art.
>
> (emphasis added)

[1] It is noted that the Abbott Declaration refers to U.S. 6,852,285 by Abbott et al. The rejection under appeal relies on U.S. 6,284,197 rather than U.S. 6,852,285. However, U.S. 6,852,285 issued from Application No. 09/898,132, which is a continuation of 09/127,382, now U.S. 6,284,197. Therefore, although the Abbott Declaration refers to U.S. 6,852,285 rather than U.S. 6,284,197, the statements made in the Declaration are equally applicable to the pending rejection as the disclosures of the two patents are the same.

The Examiner has made reference to this disclosure by Abbott et al. because this teaching indicates that the detection surface of Abbott et al. is compatible with microcontact printing techniques. The primary references, Bernard et al. and Renault et al., each used a type of microcontact printing ("affinity" microcontact printing) to stamp ligand onto a surface. The Examiner has called attention to this disclosure merely because it adds additional evidence to the record as to why one of ordinary skill in the art would have had a reasonable expectation in combining the prior art teachings to arrive at the claimed invention.

As set forth in the rejection, there are in principle at least two different ways in which one of ordinary skill in the art could have combined the teachings of Bernard et al. or Renault et al. with those of Abbott et al. in order to arrive at the claimed invention. These two ways were articulated in the rejection of record: first, one could first print the detection surfaces of Bernard et al. or Renault et al. with ligand by affinity microcontact printing (as per the methods of Bernard et al. or Renault et al.) and then subsequently apply a liquid crystal to the ligand-printed surface. Second, since claim 1 does not clearly require a particular order in which the liquid crystal is contacted with the liquid crystal, this means that the detection surface could be already contacted with the liquid crystal prior to application of the ligand. As such, one could also arrive at the claimed invention by employing the liquid crystal devices of Abbott et al. (having liquid crystal already coupled to the substrate surface) as the detection surface on which the ligand is microcontact printed (as per the affinity microcontact printing methods of Bernard et al. or Renault et al.).

The Examiner has made reference to the teaching of microcontact printing by Abbott et al. only in regards to the Second combination above. It was thought worthy of mention because it

is possible that not all types of surfaces would be capable of being subjected to microcontact printing techniques. For example, a surface might be too malleable to print onto. Therefore, the Examiner made mention of this disclosure by Abbott et al. because it indicates that one of ordinary skill in the art would have recognized that the detection surfaces of Abbott et al. would be compatible with microcontact printing. Since Bernard et al. and Renault et al. used a type of microcontact printing (affinity microcontact printing), this lends weight to the evidence of record that one of ordinary skill in the art would reasonably expect success in carrying out the Second combination above, i.e. in using the microcontact printing methods of Bernard et al. or Abbott et al. to print ligands onto the liquid crystal-containing detection surfaces of Abbott et al.

The Abbott Declaration urges that the disclosure of microcontact printing in the Abbott et al. patent is in a different context, namely that of fabrication of surfaces with small structures (i.e., printing structural regions onto the surfaces). The Abbott Declaration further argues that the Abbott et al. patent does not suggest use of microcontact printing to *deliver analytes to a surface* for detection of molecular interactions using liquid crystal. See the Declaration at item 6. In other words, Abbott et al. disclose microcontact printing for the purpose of printing structural regions when making the surface, while microcontact printing is used by Bernard et al. and Renault et al. for a different purpose, that of printing analyte regions onto a surface.

However, the rejection of record does not contend that the Abbott et al. patent suggests microcontact printing as a means of delivering analytes to a surface. It is acknowledged that the Abbott et al. patent does not teach *affinity* microcontact printing, the type of microcontact printing taught by Bernard et al. and Renault et al.

It therefore appears that Appellant and Examiner are in agreement regarding the scientific teachings of the Abbott et al. patent in regards to microcontact printing.

The disagreement apparently arises as to the impact of this teaching by Abbott et al. The rejection of record does not contend or rely on the assumption that Abbott et al. teaches affinity microcontact printing. The Examiner does not find the disclosure of "microcontact printing" by Abbott et al. to be in any way critical to the rejection. Appellant's focus on this is therefore respectfully not understood, as this disclosure by Abbott et al. is at best tangential to the rejection. Were this disclosure not present in Abbott et al., the rejections would still have been made. The Examiner made mention of this disclosure simply because it adds additional weight to the evidence that one of ordinary skill in the art would have had a reasonable expectation of success in combining the prior art teachings in the manner of the Second combination above.

Finally, it is noted that the Abbott Declaration only relates to the Second combination discussed above. Because the First combination above involves using the detection surfaces of Bernard et al. and Renault et al. and subsequently applying liquid crystal thereon, the issue of whether the Abbott et al. detection surface would be compatible with microcontact printing is moot. In the case of this First combination, a reasonable expectation of success is evident for other reasons as set forth in the rejection.

In summary, while the Abbott Declaration has been fully considered, it is seen as an attempt to rebut a factual position which has not been taken by the Office. Because the determination of obviousness does not contend or rely on the position Appellant argues against, the Declaration evidence attempting to rebut such a position is not persuasive to outweigh the evidence of obviousness.

Regarding argument **(2)** above, Appellant argues for distinctions between the detection of affinity-stamped ligand onto a detection surface by liquid crystal detection vs. detection by fluorescent or radioactive labeling, stating that these two techniques rely on completely different principles and have completely different uses (Replacement Argument Section submitted on 2/12/2009 at pages 9-11, item 3; see especially at page 9, penultimate paragraph).

It is acknowledged that the two detection methods, liquid crystal-based detection and detection by fluorescent or radioactive labeling, do have differences.

However, the prior art of record indicates that both of these detection methods were known in the art to be suitable for detecting the presence of ligands on surfaces. In particular, the teachings of Abbott et al. establish that liquid crystal detection was known in the art to be applicable to detection of ligands on a surface.

Therefore, although the two detection methods have differences, Appellant's arguments that they have completely different uses are not persuasive since both methods were in fact recognized in the art to be suitable for the same purpose.

In addition, as discussed above both detection methods were known in the art to be suitable for the purpose of detecting ligands bound to a surface. Appellant has not adequately explained why the *manner* in which the ligand is applied to the detection surface—here, by affinity stamping—would be of significance or would lead one of ordinary skill in the art to lack a reasonable expectation of success.

Appellant further argues that Bernard et al. do not teach or suggest liquid crystal detection. See Replacement Argument Section submitted on 2/12/2009 at page 9, penultimate paragraph to page 10, first line.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In the instant case, liquid crystal detection is taught in the secondary reference, Abbott et al.

Appellant further argues that Bernard et al. only teach polystyrene substrates and that similarly, Renault et al. only teach glass as a stamping substrate (Replacement Argument Section submitted on 2/12/2009 at the paragraph bridging pages 9-10). Appellant argues that no further teaching as to selection of suitable detection surfaces is provided, and certainly no expectation of success for combining affinity microcontact printing with liquid crystal detection (ibid).

As discussed above, there are in principle two ways to combine the teachings of the prior art to arrive at the claimed invention.

First, one could first print the detection surfaces of Bernard et al. or Renault et al. with ligand by affinity microcontact printing (as per the methods of Bernard et al. or Renault et al.) and then subsequently apply a liquid crystal. Second, since claim 1 does not clearly require a particular order in which the liquid crystal is contacted with the liquid crystal, this means that the detection surface could be contacted with the liquid crystal prior to application of the ligand. As

such, one could also arrive at the claimed invention by employing the liquid crystal devices of Abbott et al. (having liquid crystal already coupled to the substrate surface) as the detection surface on which the ligand is microcontact printed (as per the affinity microcontact printing methods of Bernard et al. or Renault et al.).

In the case of the First combination, the Examiner finds that one would be motivated to contact the glass or polystyrene detection surfaces taught by Bernard et al. and Renault et al. with a liquid crystal as taught by Abbott et al. In this regard, Abbott et al. indicate that glass and polystyrene are both suitable substrates compatible with liquid crystal detection (see columns 14-16). Because the detection surfaces of Bernard et al. and Renault et al. are made of the same materials taught by Abbott et al. to be suitable, it is maintained that one of ordinary skill in the art would have had a reasonable expectation of success in employing the detection surfaces of Bernard et al. and Renault et al. with liquid crystal detection.

In the case of the Second combination, the application of ligand onto the liquid crystal-containing detection surfaces of Abbott et al. by the affinity microcontact printing methods of Bernard et al. or Renault et al. is seen to represent simply a different way of delivering the ligand to the surface. As discussed above, based on the evidence of record the Examiner does not see why the *manner* in which the ligand is applied to the detection surface—here, by affinity stamping—would be of significance or would lead one of ordinary skill in the art to lack a reasonable expectation of success.

Appellant further argues that Abbott et al. does not show or suggest that detection surfaces may also act to receive a ligand to be detected from an affinity substrate (Replacement Argument Section submitted on 2/12/2009 at page 10, first paragraph).

This is not found persuasive because it amounts to a piecemeal analysis of the references. In the instant case, delivery of ligands to surfaces by affinity stamping is taught by the primary references, Bernard et al. and Renault et al.

Appellant again argues that the discussion of "microcontact printing" by Abbott et al. is in a different context, i.e. in the context of printing patterns or regions on a surface rather than in the context of printing ligands or analytes onto regions of a surface by *affinity* microcontact printing (Replacement Argument Section submitted on 2/12/2009 at page 10, second paragraph to page 11, first paragraph).

Appellant's arguments are not persuasive for the reasons set forth above (see response to the arguments pertaining to the rejections under 112, 2nd paragraph).

In particular, it is acknowledged that Abbott et al. does not disclose the specific type of microcontact printing used by Bernard et al. or Renault et al. (*affinity* microcontact printing). It is further acknowledged that Abbott et al. does not direct the skilled artisan to employ microcontact printing for the purpose of delivering ligands or analytes to surfaces. The rejection of record does not contend to the contrary.

Therefore, Appellant's identification of this issue as "central" is respectfully not understood, as this line of argument and the Abbott Declaration are considered to represent attempts to rebut a position which has not been taken by the Office.

However, it is maintained that this disclosure by Abbott et al. does lend additional weight to the evidence that one of ordinary skill in the art would have had a reasonable expectation of success in using the affinity microcontact printing methods of Bernard et al. or Renault et al. with the detection surfaces of Abbott et al. In particular, it is maintained that the teaching at issue does indicate that the detection surfaces of Abbott et al. are compatible with microcontact printing techniques. As affinity microcontact printing is a type of microcontact printing, a person of ordinary skill in the art would have reasonably expected success in using affinity microcontact printing with the detection surfaces of Abbott et al.

It is further noted (as discussed further above) that such arguments regarding the disclosure of "microcontact printing" by Abbott et al. are at best applicable to the Second identified way to combine the reference teachings. Appellant's arguments in this regard therefore fail to address the First combination (i.e., contacting the detection surfaces of Bernard et al. or Renault et al. with liquid crystal).

Appellant further argues that a successful result could not have been predicted "due to the lack of available guidance in the art for combining affinity microcontact printing with liquid crystal detection" (Replacement Argument Section submitted on 2/12/2009 at the paragraph bridging pages 10-11; see also at page 11, numbered item 4, last sentence).

However, Appellant has not adequately documented evidence of unpredictability or explained in what way unpredictability is relevant to the facts of the instant case. Applicant has not documented, for example, specific scientific facts necessary that were unknown in the art or

specific technical obstacles it was necessary to overcome in order to successfully combine liquid crystal detection with affinity microcontact printing.

Therefore, the general argument by counsel that guidance was not available, in the absence of specific scientific reasoning or factual details to support this argument, is not found persuasive to outweigh the evidence of obviousness.

Regarding argument **(3)** above, Appellant argues that there is simply no teaching, suggestion or motivation in the cited documents or in the knowledge generally available to the artisan that would have led the artisan to combine the prior art teachings to arrive at the claimed invention (Replacement Argument Section submitted on 2/12/2009 at page 11, numbered item 4).

The Examiner disagrees for reasons of record as set forth in the rejection. In particular, Abbott et al. teach that liquid crystal detection surfaces do not require prelabeling of the ligand to be detected (as was performed in Bernard et al. and Renault et al.). As such, one would be motivated to combine the prior art teachings in order to avoid the need to use radioactive or other labels on the ligands. In addition, Abbott et al. teach that liquid crystal detection produces an easily detectable optical output that can even be detected by the naked eye. Therefore, one would also be motivated to employ liquid crystal detection of ligands printed by the methods of Bernard et al. or Renault et al. for ease of detection.

Regarding argument **(4)** above, Appellant argues impermissible hindsight because of the lack of guidance in the cited documents and in the art at the time of the invention (Replacement Argument Section submitted on 2/12/2009 at pages 11-12, numbered item 5.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As discussed above, Appellant has not sufficiently explained or documented what necessary guidance is lacking; the general argument by counsel that guidance is lacking is not found persuasive to outweigh the evidence of obviousness.

Appellant does not separately argue the limitations of dependent claims 2-6, 8-11, 13, 15-20 or 22-23 (see Replacement Argument Section submitted on 2/12/2009 at page 11, second paragraph).

Regarding the rejections of dependent claims 14 and 21 under § 103, the Reply Brief includes separate sections corresponding to these rejections (see Replacement Argument Section submitted on 2/12/2009 at pages 12-13, sections C and D) but Appellant does not separately argue the limitations of the dependent claims.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Christine Foster/

Examiner, Art Unit 1641

Conferees:

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643